REMARKS

The specification at paragraph [0001] has been amended to update the status of the parent application in view of the objection by the Patent Office. Entry of the amendment and withdrawal of the objection are respectfully requested.

Claims 3-5, 20-23 and 32-35 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Several corrections have been suggested in the identified claims, *e.g.*, the lack of an antecedent basis and correction in line 1 of claims 3-5, an editorial change to claim 20, a change to the subject of claims 21-23 and an explicit recitation in claim 32 for the abbreviation "AHS" to establish its meaning. Furthermore, the Office notes that it is not clear whether the recited percentages in claim 32 refer to weight or volume percentages. However, it is respectfully noted that the claim already includes the recitation "by weight" in line 5, immediately preceding "(a)." Withdrawal of this aspect of the rejection is respectfully requested. Entry of these editorial corrections and withdrawal of the rejections are respectfully requested. Amendments to the claims referred to in this paragraph are not intended to be narrowing, and no narrowing has been effected.

Paragraphs 5 and 6 of the instant Office Action state the following rejections: (5) Claims 1-5, 15-16 and 19-21 are rejected under the judicially-created doctrine of obviousness-type double patenting as being unpatentable over claims 8-10, 12-13, 24-25, 27-31 and 40-41 of U.S. Patent No. 6,773,924 in view of *Kararli et al.*, Published U.S. Application No. 2003/0078266; and (6) Claims 1-5, 24-27 and 30-31 are provisionally rejected under the judicially-created doctrine of obviousness-type double patenting as being unpatentable over claims 17, 19, 21, 25-26, and 42-43 of copending Application No. 10/858,163 in view of *Kararli et al.*, Published U.S. Application

No. 2003/0078266. As suggested by the Patent Office, these rejections can be overcome by a timely filed terminal disclaimer and an appropriate terminal disclaimer directed to the rejection in Paragraph 5 accompanies the present amendment. The Office Action notes that the rejection in Paragraph 6 is provisional because the conflicting claims in the recited co-pending application have not in fact been patented. It is respectfully noted that, at such time as either the claims of the present or co-pending application have been granted, a suitable terminal disclaimer will be entered in the then-pending application in order to obviate an obviousness-type double patenting rejection. Withdrawal of these rejections is respectfully requested.

Claims 1-43 are rejected under 35 U.S.C. § 103(a) as being anticipated by *Lehmann et al.* (WO 99/07401, the English-language equivalent of which is U.S. Patent No. 6,372,715, submitted in the IDS filed May 14, 2004) in view of *Kararli et al.* For a teaching of *Kararli et al.*, the Patent Office refers to earlier paragraphs of the instant Office Action. In paragraph 9 of the Office Action, the Patent Office explains that *Lehmann et al.* teach of a composition suitable for parenteral administration to a patient which comprises an iron complex as the active substance. It is further explained that the iron complex can be sodium iron (III) gluconate complex, which qualifies as a sodium ferric gluconate complex. Preferred iron preparations are said to be Fe(II) complexes, especially those with a molecular weight of between 30,000 and 100,000 Daltons. Fe(III) saccharate is especially preferred. (The Office identifies column 3, lines 58-67 and column 4, lines 1-10 of the cited patent.) It is further stated that the iron preparation can be present in a solid form such as a lyophilized form, and at the time of use the lyophilizate can be reconstituted with a liquid such as a pharmaceutical usual injection media. (Column 5, lines 42-51 and column 6, lines

30-36 of the cited patent.) Furthermore, it is stated that the composition containing the iron complex can be used alone as an individual composition in a powder form held within an individual unit container such as a glass ampoule. (Column 5, lines 52-65 and column 6, lines 27-36 of the cited patent.) Finally, it is stated that the iron composition can also be used to treat iron metabolism disorders by reconstituting the lyophilized powder composition with a liquid and administering the composition parenterally to a subject. (Column 7, lines 52-55 of the cited patent.) The Patent Office acknowledges that *Lehmann et al.* fail to teach of a parenterally acceptable buffering agent in the composition and *Kararli et al.* is apparently relied on to cure this deficiency. This rejection is respectfully traversed.

It is initially noted that the invention in *Lehmann et al.* is not directed to "an iron complex as the active substance," but, rather, to a combination therapy comprising erythropoietin (EPO) in combination with an iron preparation. This distinction is significant since *Lehmann et al.* merely discloses and uses the then available, commercial, oral iron preparations as described in column 3, lines 25-34. The further description in *Lehmann et al.* of properties for such ferric complexes, appearing at column 4, lines 1-19, is taken from the published information relating to these commercially available compositions, also as noted by *Lehmann et al.* with regard to "Ferrum Vitis." Additionally, *Lehmann et al.* mischaracterizes the molecular weight of the commercial product "Ferrlecit" as being "about 1000 Daltons." (Col. 4, ln. 15.) Ferrlecit has been described in detail in the present application and its molecular weight properties are reported herein; *see, e.g.*, paragraph 0004. As an aside, it is noted that if Ferrlecit had a molecular weight of about 1000 Daltons, all of it would be a low molecular weight impurity removed by the process described

in the present application, leaving no active hematinic species. Consequently, the molecular weight value recited in the reference has been disregarded for purposes of this response.

Although several portions of *Lehmann et al.* are identified, the disclosure appearing in *Lehmann et al.* at column 5, lines 38-51 appears to have been considered especially relevant and it is quoted in full as follows:

> When using the combination preparations, it is possible to administer the preparations, preferably the EPO preparation and the iron preparation, in a so-called fixed combination, i.e. in a single pharmaceutical formulation in which the compounds are present. This can comprise, e.g. injection solutions, infusion solutions or lyophilizates, which, for example are filled into ampoules. This administration form has the advantage that the EPO preparation is stabilized by the iron complex during the production and the storage of the administration form. The fixed combination of the active substances in the form of a lyophilizate has the further advantage of simple and safe handling. The lyophilizate is dissolved in the ampoule by the addition of pharmaceutically usual injection media and administered intravenously.

It is further stated in *Lehmann et al.* at col. 6, lns. 30-33 that the iron preparation can be present in solid form (tablet, powder, granulate, lyophilizate, etc.) or also in liquid form in a separate container.

While these disclosures superficially appear to relate to the rejected claims, there are significant distinguishing factors. First and foremost, *Lehmann et al.* provide no teaching, suggestion, or example relating to the production of a lyophilized iron preparation *per se*. In fact, the sole example in *Lehmann et al.*, Example 1, column 11, refers only to the i.v.

(intravenous) administration of "iron sucrose." In the absence of any further description, it is assumed that the "iron sucrose" referred to is one of the commercially available iron preparations described at columns 3 and 4, even though "iron sucrose" is not explicitly identified in those columns. In any event, while *Lehmann et al.* refer to the *desirability* of a lyophilized form of an iron preparation, there is no disclosure of any means for actually producing a lyophilized iron preparation, nor was (or is) such a material commercially available. Applicants are the first to have disclosed the method by which such a material can be produced and the first to have achieved production of such a product.

Furthermore, as described in the present application beginning at paragraph [0081], producing a lyophilized active hematinic substance is particularly difficult, and prior to the present application, no reference has been identified that teaches the preparation of a lyophilized iron composition suitable for parenteral administration. As additional support for this position, and, as previously explained by Dr. Beck during the course of an interview of record during prosecution of related grandparent patent, U.S. Patent No. 6,537,820, enclosed herein is a copy of the Declaration previously submitted pursuant to 37 C.F.R. §132 by co-inventor Dr. Robert Beck, describing his attempt to lyophilize a commercial sample of Ferrlecit that was unsuccessful and resulted in a "sludge-like" material. In contrast, by following the teachings of the present application, Dr. Beck was able to produce a lyophilized or freeze-dried active hematinic composition in powdered form. The mere implication in *Lehmann et al.* that such a composition would be desirable without teaching how to produce it is recognized as not being a teaching in fact. Further in this regard, the Patent Office's attention is invited to MPEP 2121.02 entitled *Compounds and Compositions —— What*

Constitutes Enabling Prior Art —— 2100 Patentability. In contrast, the present application discloses the technology necessary for producing the claimed lyophilized active hematinic species.

It is respectfully noted that the deficiencies of *Lehmann et al.* significantly exceed the mere failure to teach of a parenterally acceptable buffering agent in the composition. As discussed above, *Lehmann et al.* fail to teach any means by which at least one active hematinic species in powder form can be produced. Absent such a teaching, reference in *Kararli et al.* to the use of a buffering agent in a parenteral composition that allows a pH to be established that is consistent with the therapeutic drug or agent present in the composition and provides a medium where the therapeutic drug or agent is chemically stable is inadequate to compensate for the more significant failings of *Lehmann et al.* Furthermore, it is observed that *Kararli et al.* is directed to a different class of drugs, namely COX-2 inhibitors, that are totally unrelated both chemically and physically to the parenterally administered iron-saccharidic complexes of the present invention and there is no suggestion that the teachings of *Kararli et al.* are universally applicable to all drugs, either with regard to the preparation of a lyophilized form of the drug or to its buffering. Furthermore, as described in the present application and in the Declaration of Dr. Beck referred to above, the commercially available hematinic compositions disclosed in *Lehmann et al.* are not suitable for lyophilization. Consequently, it is respectfully suggested that both the underlying teachings of *Lehmann et al.* and the additional teachings of *Kararli et al.* are inadequate to provide an appropriate basis under 35 U.S.C. § 103(a) for rejecting claims 1-43 of the instant application. Withdrawal of this rejection is respectfully requested.

As it is believed that all of the rejections set forth in the Official Action have been fully met, favorable reconsideration and allowance are earnestly solicited.

If, however, for any reason the Examiner does not believe that such action can be taken at this time, it is respectfully requested that she telephone Applicants' attorney at (908) 654-5000 in order to overcome any additional objections which she might have.

If there are any additional charges in connection with this requested amendment, the Examiner is authorized to charge Deposit Account No. 12-1095 therefor.

Dated: February 22, 2005

Respectfully submitted,

By _____

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